REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

In the specification, paragraphs have been amended on pages 1, 15, 51, and 60. The amendment on page 1 is to correctly claim priority. The other amendments are for the purpose of removing hyperlinks from the specification.

Claims 3-5 and 11 are currently being amended. Exemplary support for the amendments to the claims is found throughout the specification. *See, e.g.,* page 4, lines 30-33.

Claims 94 and 95 are currently being added. Exemplary support for the newly added claims is found in the specification on page 22, lines 11 and 28. Newly added claims 94 and 95 are added to further define claim scope.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 1-95 are now pending in this application and claims 1, 2, 8-10, 13-43, 45-84 and 86 are withdrawn. Thus, claims 3-7, 11, 12, 44, 85, and 87-95 are being examined.

A. Unity

The examiner has found Applicants' arguments for unity of invention unpersuasive and makes the election requirement final. Specifically, the examiner has withdrawn claims 1, 2, 8-10, 13-43, 45-84 and 86 and is examining claims 1, 2, 8-10, 13-43, 45-84 and 86 on the merits. Applicants respectfully traverse for reasons already of record.

B. Priority

Applicants acknowledge that the examiner has found SEQ ID NOS: 2 and 17 supported by provisional application no. 60/144,992, to which the present application claims priority.

C. Specification/Informalities

Applicants thank the examiner for withdrawing the objection identified as item [2] in the Office action mailed June 15, 2004 based on the amendment filed July 7, 2004.

The examiner has further objected to the specification as improperly incorporating by reference subject matter identified by reference to a hyperlink. The references to hyperlinks are being removed by amendment. However, Applicants reserve the right to amend the specification to include any essential material included at the hyperlinks as permitted by MPEP § 608.01(p)(I)(A)(2), if necessary.

The examiner further objects to the specification, because it is argued that the title is not descriptive. The examiner suggests changing the title to "Human Polynucleotide Encoding a Polypeptide Homologous to Fatty Acid Coenzyme A Ligase 5."

Applicants respectfully disagree, but agree to change the title to expedite prosecution. Applicants suggest that the title be changed to recite "Polynucleotides Encoding Polypeptides Homologous to Human Fatty Acid Coenzyme A Ligase 5." This proposed title is "brief but technically accurate and descriptive" as required by MPEP § 606.

D. Declaration

The examiner notes that the amendment to the specification filed July 7, 2004 indicates that the present application claims priority to provisional application no. 60/144,992, but the declaration indicates that the present application claims priority to both provisional application nos. 60/144,992 and 60/168,858. The examiner suggests correcting the declaration accordingly.

Applicants appreciate the examiner's suggestion. However, the declaration is correct, and the amendment made to the specification filed July 7, 2004 was an error. The present application should claim priority to both provisional application nos. 60/144,992 and 60/168,858 as indicated on the face of the parent PCT application and the papers filed with the present application. An appropriate amendment to the specification is being made with this reply to correct the discrepancy.

E. Claim Objections

Claims 3-7, 12, 85, and 87-93 are objected to as being dependent on claims drawn to a non-elected invention. Claims 5 and 11 are objected to as reciting non-elected matter. Applicants have amended the claims, so claims 3-7, 12, 85, and 87-93 are no longer dependent on claims drawn to a non-elected invention nor do the claims recite non-elected matter.

F. Claims Rejections – 35 U.S.C. § 101

Claims 3-7, 11-12, 44, 85, and 87-93 are rejected under 35 U.S.C. § 101, because the examiner argues that the claims are not supported by either a substantial asserted utility or a well-established utility. Applicants respectfully disagree with the examiner's findings and respectfully request reconsideration and withdrawal of the rejection.

MPEP § 2107(II) states that "an applicant need only provide one credible assertion of specific and substantial utility for each claimed invention." Additionally, an applicant needs to "establish a probative relation between the submitted evidence and the originally disclosed properties of the claimed invention." On the basis of the above recited MPEP sections, the original specification and the attached publication, applicants argue that the subject matter of the present application possesses specific and substantial utility as required under 35 U.S.C. § 101.

As noted by the examiner, the specification asserts that the claimed nucleotides are useful "in the diagnosis, treatment, and prevention of immune, neuronal, and reproductive disorders, and cell proliferative disorders, including cancer" at page 1:6-8. The specification more specifically recites utility for SEQ ID NO: 17 in Table 3 (page 76). The table shows

that SEQ ID NO: 17 is expressed in gastrointestinal, reproductive, and hematopoietic tissue and is associated with cancer, inflammation, and cell proliferative diseases, disorders, and conditions. The specification includes extensive teachings of how the present invention provides therapeutics and diagnostics. *See* Spec. at 34-55. This utility is supported by the attached references.

Yamashita *et al.*, *Fatty acid induced glioma cell growth is mediated by the acyl-CoA synthetase 5 gene located on chromosome 10q25.1-1-q25.2, a region frequently deleted in malignant gliomas*, ONCOGENE 19:5919-25 (2000) (Exhibit B) discusses an acyl-CoA synthetase ACS5. ACS5 is nearly identical to SEQ ID NO: 2 as shown in Exhibit A. Yamashita *et al.* demonstrates that ACL5 mediates "a novel growth induction of glioma cells." Yamashita *et al.* at 5921, col. 2. The reference further suggests that ACL5 "may be of pathological significance for the development and progression of malignant gliomas." *Id.* In other words, ACL5 is shown to be involved in brain cancer. This supports the claimed utility of SEQ ID NO: 17 for use "in the diagnosis, treatment, and prevention" of cancer.

Oikawa *et al.*, *A Novel Acyl-CoA Synthetase, ACS5, Expressed in Intestinal Epithelial Cells and Proliferating Preadipocytes*, J. BIOCHEM. 124(3):679-85 (1998) (Exhibit C) discloses that ACL5 is "abundantly expressed in intestinal epithelial cells." Oikawa *et al.* at 683, col. 2. ACL5 is also shown to be present in proliferating preadipocytes unlike other acyl-CoA synthetases. *Id.* Therefore, this reference supports the claim that SEQ ID NO: 17 is expressed in gastrointestinal tissue and involved in cell proliferation and that SEQ ID NO: 17 is useful for diagnosing and treating cell proliferative diseases and conditions.

Gassler *et al.*, *Impaired Expression of Acyl-CoA-Synthetase 5 in Epithelial Tumors of the Small Intestine*, HUMAN PATHOLOGY 34(10):1048-52 (2003) (Exhibit D) shows that ACS5 is found predominantly in the small intestine, i.e., a "gastrointestinal" tissue and is expressed in an altered pattern in tumors. *See* Abstract. Thus, this teaching supports the specification's teaching of diagnostics and treatments for cancer, and especially gastrointestinal cancer.

In light of the above identified uses for the claimed protein sequence compositions, applicants argue that the subject matter of the claimed invention discloses at least "one credible assertion of specific and substantial utility" and thus, satisfies the requirements of 35 U.S.C. § 101. Therefore, Applicants argue that this rejection should be withdrawn and the present claims allowed.

G. Claim Rejections 35 U.S.C. § 112, ¶ 2 (Indefiniteness)

Claims 3-7, 11, 12, 85, 87-93 are rejected under 35 U.S.C. § 112, ¶ 2 as being indefinite or being dependent on an indefinite claim. The specific rejections are addressed below.

a. Recitation of "biologically active"

Claim 3 and its dependent claims 6-7 are rejected as being indefinite based on the recitation of "biologically active." The examiner believes the term to be vague and unclear. Applicants respectfully disagree. However, to expedite prosecution, Applicants have amended the claims to recite "a biologically active fragment of SEQ ID NO: 2 having synthetase activity." Thus, Applicants respectfully request the rejection be withdrawn.

b. Improper Alternative Expression

Claims 3 and its (6-7 dependent therefrom), 4-5, and 11 (claims 12, 85, and 87-93 dependent therefrom) are rejected as reciting an improper alternative expression. The examiner suggests amending the claims to recite "selected from the group consisting of" where "and" is inserted prior to the last recited member of the Markush group.

Applicants have amended the claims, so "and" precedes the last recited member of any Markush group. Thus, Applicants respectfully request the rejection be withdrawn.

c. Recitation of "specifically hybridizable"

Claim 87 and its dependent claims 88-93 are rejected, because it is argued that the term "specifically hybridizable" is unclear and fails to recite the hybridization conditions. Specifically, the examiner argues that the claim lacks a description of the sequence similarity

required for hybridization and lacks a statements of acceptable hybridization conditions making the claim indefinite. Applicants respectfully traverse.

The specification clearly defines hybridization on page 17, lines 1-31. This definition includes a description of different hybridization conditions and experimental parameters. For example, the specification states that "[p]ermissive conditions for annealing of nucleic acid sequences are routinely determinable for one of ordinary skill in the art...." Spec. at 17:7-9; *see also* spec. at 25:18-23. The specification further gives examples of annealing conditions and wash conditions for "[h]igh stringency conditions." Spec. at 17:21-31. In other words, the specification teaches that permissive conditions are routinely determined by one of ordinary skill in the art depending on the application and gives examples of such conditions. Thus, the term "specifically hybridizable" is clearly defined in the specification and is clear and concise to one of ordinary skill in the art. Applicants respectfully request the rejection be withdrawn.

H. Claim Rejections – 35 U.S.C. § 112, ¶ 1

A number of claims have been rejected as failing to comply with different 35 U.S.C. § 112 requirements. The specific rejections are addressed below.

a. Written Description

Claims 3, 6-7, 11-12, 85, and 87-93 are rejected as failing the satisfy the written description requirement. The examiner argues that the claims contain subject matter not described in the specification in such a way as to reasonable convey that Applicants had possession of the invention at the time of filing. Specifically, the examiner argues that the claims cover a genus while the specification discloses only a specific species. Applicants respectfully traverse.

The specification provides sufficient disclosure to reasonably convey that Applicants were in possession of the claimed invention at the time of filing. In addition to the specific sequences provided, i.e., SEQ ID NOS: 2 and 17, the specification provides structural and functional information about the sequences. For example, Table 2 provides potential phosporylation and glycosylation sites, signature sequence characteristics, and homologous

sequences to SEQ ID NO: 2. See Spec. at 71. Table 3 provides tissues, conditions, and diseases associated with SEQ ID NO: 17. Spec. at 76. This additional information gives structural and functional definitions of the specifically recited sequences. For example, the signature sequences and glycosylation and phosphorylation sites teach structural information, and the homologous sequences teach the biological function of the claims sequences. The specification also teaches a number of methods to obtain sequences related to the specifically recited sequences. See e.g. spec. at 25:13-17; 26:3-23; 27:7-36-28:31. Thus, the specification contains extensive functional and structural descriptions of the specifically recited sequences to demonstrate possession of the invention at the time of filing.

Further, Applicants amended the claims to recite both structural and functional limitation. For example, claim 3 (b) was amended to recite "an amino acid sequence having at least 90% sequence identity to SEQ ID NO: 2 and having synthetase activity."

The examiner also argues that the specification fails to provide characteristics that distinguish "naturally occurring" polynucleotides from other polynucleotides. Applicants respectfully disagree. However, to expedite prosecution, applicants deleted the term "naturally occurring" and added "having synthetase activity".

In light of the structural and functional descriptions of the specifically recited sequences, the specification clearly demonstrates possession of the invention at the time of filing. Thus, Applicants respectfully request that the written description be withdrawn.

b. Enablement

Claims 1-6, 8, 10-11, and 15 are rejected by the examiner under 35 U.S.C. § 112, ¶ 1, because the examiner states that the claimed invention is supported by neither a substantially asserted utility or a well established utility. As set forth above, Applicants assert that the present application provides a specific and substantial as well as a well-established utility for the claimed invention. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection.

Even if these rejections can be overcome, the examiner maintains that the claims are not enabled. Specifically, the examiner argues that the specification enables an isolated nucleic acid encoding SEQ ID NO: 2, but the specification does not enable "all variants of SEQ ID NO:17 and polynucleotides encoding polypeptides comprising variants and fragments of SEQ ID NO:2 as encompassed by the claims." The examiner concludes that undue experimentation would be required based on an analysis of certain factors articulated in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Applicants respectfully disagree, because an *In re Wands* analysis actually demonstrates that the claims do not require undue experimentation.

Claims are not properly enabled if undue experimentation is required by one of ordinary skill in the art in order to obtain the claimed invention. Certain factors relevant to determining whether or not undue experimentation is required were articulated in *In re Wands* as follows: (a) The breadth of the claims; (b) The nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988); MPEP § 2164.01. It is improper to focus on a single factor, but a determination that undue experimentation is required must be based on the evidence as a whole. See MPEP § 2164.01. Even if complex experimentation is required, the claims experimentation is not necessarily undue. See *Id.*

1. Claim Scope

The claims are limited to the recited sequences and sequences with at least 90% identity and having synthetase activity or some specifically defined function. Thus, the claims are limited to specifically defined sequences and sequences with specifically defined characteristics.

2. State of the Art

The state of the art is high. Genetic engineering has largely become an automated process with computer controlled machinery performing routine tasks, such as

sequencing and sequence comparisons. In addition, methods of producing synthetic polynucleotides and recombinant proteins, isolating polynucleotides, and determining biological function are routine tasks. While it is true that single amino acid substitutions can significantly alter the function of proteins, techniques for screening biological activity are routine. Just because complex experimentation is required does not mean that undue experimentation is required. See MPEP § 2164.01.

3. Level of Skill in the Art

The level of skill in the art is high. One of ordinary skill in genetics and proteomics likely has a doctorate level education and at least some practical experience. This experience includes both the extensive research needed to complete a doctorate degree and the years of industry or post-doctorate research experience possessed by one of ordinary skill in the art.

4. Predictability in the Art

The predictability in the art is moderate to high. Single substitutions can alter the function of a polypeptide. However, the specification provides examples of signature motifs. See Table 2, p. 71. In addition, methods of obtaining polynucleotides, expressing the polynucleotides to obtain polypeptides, and screening the polypeptides for activity are routine as discussed above in "State of the Art." Thus, the predictability in the art is only moderate to high, but the specification provides extensive guidance to be used with the methods routine to one of ordinary skill in the art.

5. Working Examples

The specification discloses a number of examples to guide one of ordinary skill in the art. See spec. at 55-67. These examples provide extensive guidance starting from building a cDNA library and going through sequencing, analysis, expression, and functional analysis of the polypeptides encoded. Table 2 provides specific information on structural features characteristic of the claimed sequences. The examples and structural and functional information found in Table 2 allow one of ordinary skill in the art to obtain the claimed invention with an expectation of success using routine experimental techniques.

In summary, the specification contains extensive guidance to one of skill in the art. Various techniques and methods are taught to obtain the claimed sequences and screen polypeptides for desired function. In addition, the specification teaches specific structural and functional characteristics of the claimed sequences to guide one of ordinary skill in the art. Thus, the experimentation needed to obtain the claimed invention is merely routine. Applicants respectfully request that the enablement rejection be withdrawn.

I. Double Patenting

Claims 3, 6-7, 11-12, 85, and 87-90 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 7-9, and 23-24 of copending U.S. Application No. 10/098,841. Applicants respectfully request that the examiner hold this provisional rejection in abeyance until claims are found to be allowable in one of the applications.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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